REMARKS

The following remarks are in response to the Examiner's Office Action mailed on December 3, 2003. Claim 1, 12 and 23-25 have been amended. Claims 1-26 are pending.

I. Rejection Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 1-26 under 35 U.S.C. §112, second paragraph, as being indefinite. Specifically, the Examiner states that in step (c) "detecting resolution of said four-way complex as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype" is confusing.

In response, Applicants amend step (c) of independent claims 1, 12, 23, and 25 to include "detecting resolution of said four–way complex into two duplex nucleic acids as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype of said reference polynucleotide sequence at said site of the polymorphism". Withdrawal of the rejection under 35 U.S.C. §112, second paragraph is therefore respectfully requested.

II. Rejection Under 35 U.S.C. 103(a) over Yang et al.

The Examiner has rejected claims 1-26 under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (U.S. Pat. No. 6,653,079, issued Nov. 25, 2003, filed March 12, 2001 with the earliest priority date of March 11, 2000) in view of Wu et al. (Nucleic Acids Research (1998) Vol. 26, pages 5432 –5440), Kumar et al. (Nucleic Acids Research (1998) Vol. 26, pages 831-838), or Giesen et al. (Nucleic Acids Research (1998) Vol. 26, pages 50-4-5006).

Applicants hereby state that Yang et al. cannot be used as a 102(e) reference in making a 103(c) rejection because the invention was commonly owned at the time the invention of this application was made. Under 35 U.S.C. §103(c), MPEP 715.01(b) provides:

> Where, however, a rejection is applied under 35 U.S.C. 102(f)/103 or 35 U.S.C. 102(g)/103, or, in an application filed on or after November 29, 1999, under 35 U.S.C. 102(e)/103 using the reference, a showing that the invention was commonly owned, or subject to an obligation of assignment to the same person, at the time the later invention was made would preclude such a rejection or be sufficient to overcome such a rejection.

Applicants submit here with a copy of the assignment recorded in Yang et al. to show that the invention of Yang et al. was commonly owned by FreshGene, Inc. at the time when the claimed invention of the present invention was made.

In view of this showing of common ownership of Yang et al. and the claimed invention Applicants submit that Yang et al. is not a prior art under 35 U.S.C. §103(c). Since Yang et al. is cited as the primary reference and none of the secondary references teaches or suggests the claimed invention, withdrawal of the rejection 35 U.S.C. §103(a) is respectfully requested.

III. Rejection Under 35 U.S.C. 103(a) over Lishanski et al.

The Examiner has rejected claims 1-26 under 35 U.S.C. 103(a) as being unpatentable over Lishanski et al. (U.S. Pat. No. 6,232,104) in view of Wu et al., Kumar et al., or Giesen et al.

Independent claim 1, 12, and 23 as amended specify a method for determining the genotype at the site of a polymorphism in a target polynucleotide sequence. The method utilizes a pair of partial duplexes: the first one comprising a **target** (or **mutated target**) polynucleotide sequence and the second one comprising a **mutated reference** (or **reference**) polynucleotide; or the first and second partial duplexes comprising a **mutated target** and **mutated reference** polynucleotide, respectively. The claims also specify that the a **mutated reference** (or **mutated target**) polynucleotide sequence is identical to a reference polynucleotide everywhere except at the site of a mutation that is not at the site of the polymorphism. According to claim 1, the reference polynucleotide sequence corresponds to the target polynucleotide sequence and has a known genotype at the site of the polymorphism.

In contrast, Lishanski et al. teaches detecting a difference between two related nucleic acid sequences (e.g., single nucleotide polymorphism) using a pair of partial duplexes that are identical except for the targeted difference. See *Abstract,* and Figure 1A and its legend. According to Lishanski et al., in Figure 1A partial duplexes A' and B' are related in that their hybridized portions are identical except for mutation M in partial duplex A'. Column 12, lines 49-51. The mutation M is the targeted site with a difference between the two related partial duplexes A' and B'. Thus, Lishanski et al. does not teach the claimed method that uses a pair of

partial duplexes with the target or reference sequence having a mutation **not** at the targeted site of the polymorphism.

Lishanski et al. also fails to suggest or motivate one of ordinary skill in the art to modify its method to arrive at the claimed invention. The claimed method utilizes a reference (or target) sequence that has a mutation not at the targeted site of the polymorphism. But if the target polynucleotide sequence and the reference polynucleotide sequence share the same genotype at the site of the polymorphism, the four–way complex formed by the two partial duplexes will resolve into two duplex nucleic acids.

In contrast, Lishanski et al. teaches that

> The complex [formed by the two partial duplexes] dissociates into normal duplex structures by strand exchange by means of branch migration when the double stranded portions of each partial duplex are **identical**. However, where **there is a difference between the two double stranded portion, the complex does not dissociate** and can be detected as an indication of the presence a difference between the nucleic acids.

Column 5, lines 61-64, emphasis added. Thus, this reference suggests that in order to detect a difference between the target and reference sequences, the sequences other than the targeted site need to remain identical.

Further, Lishanski et al. cautioned that creating two partial duplexes that are entirely different would destroy the purpose of the invention—detection of mutation in the target nucleic acid. Specifically, Lishanski et al. teaches that

> Since the target-related double-stranded portions of the quadramolecular complex produced from the combination of partial duplexes produced by specific and non-specific priming are **entirely different**, such complexes cannot exchange strands and dissociate into labeled full duplexes. The stable quadramolecular complexes are detectable, and thus generate a signal that is related to **non-specific priming but not to the presence of a mutation.**

Column 26, lines 57-64, emphasis added. Thus, Lishanski et al. fails to motivate one of ordinary skill in the art to use a target or reference sequence that has a mutation not at the targeted site of polymorphism.

None of the secondary references, Wu et al., Kumar et al., and Giesen et al., supplies the claim elements missing in Lishanski et al. As acknowledged by the Examiner, Wu et al. merely teaches introduction of a GC-rich sequence; Kumar et al. a duplex with minor groove binding motif; and Giesen et al. duplexes with PNAs. In view of the failure of the cited references to teach or suggest all of the claim elements, Applicants submit that a prima facie case of obviousness has not been established under 35 USC 103(a). Withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: April 5, 2004 By: _____

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